EXHIBIT C

H

Ajinomoto Co. Inc. v. Archer-Daniels-Midland Co.
D.Del.,1996.

Only the Westlaw citation is currently available.

United States District Court, D. Delaware.

AJINOMOTO CO. INC., Plaintiff,

v.

ARCHER-DANIELS-MIDLAND CO., Defendant.

CIV. A. No. 95-218-SLR.

Oct. 21, 1996.

Kent A. Jordan, and Peter A. Pietra of Morris, James, Hitchens & Williams, Wilmington, DE, for plaintiff (Arthur I. Neustadt, Marc R. Labgold, William J. Healey, and Catherine B. Richardson of Oblon, Spivak, McClelland, Maier & Neustadt, P.C., Arlington, VA; Thomas Field, and Lawrence Rosenthal of Strook & Strook & Lavan, New York City, of counsel).

Jack B. Blumenfeld, and Thomas C. Grimm of Morris, Nichols, Arsht & Tunnell, Wilmington, DE, for defendant (Charles A. Laff, John T. Gabrielides, Kevin C. Trock of Laff, Whitesel, Conte & Saret, Ltd., Chicago, IL; J. Alan Galbraith, and Ari S. Zymelman of Williams & Connolly, Washington, DC, of counsel).

MEMORANDUM OPINION

SUE L. ROBINSON, District Judge.

I. INTRODUCTION

***1** Plaintiff Ajinomoto Co., Inc. ("Ajinomoto") filed this suit against defendant Archer-Daniels-Midland Co. ("ADM") on April 6, 1995, alleging willful infringement by ADM of claims 1-4 of U.S. Patent No. 4,278,765 ("the '765 patent"), entitled "Method for Preparing Strains Which Produce Amino Acids." Before the court are various motions for summary judgment on the issues of infringement, validity and enforceability. The court has jurisdiction over this matter pursuant to 28 U.S.C. § 1338(a).

II. BACKGROUND

A. The '765 Patent

The object of the invention claimed in the '765 patent is

> to use genetic engineering techniques to prepare strains which produce aminoacids [sic] possessing enhanced capability of producing aminoacids without additional growth factors.

(D.I. 194, Ex. A, col. 3, lines 1-4) Claims 1 and 2 FN1 of the '765 patent are generic claims, drawn to a method of producing a microorganism capable of producing any amino acid. Claims 3 and 4 FN2 are specifically drawn to methods of producing strains capable of producing threonine, one of the twenty naturally occurring amino acids. Claim 1 is the only independent claim; claims 2-4 depend on claim 1.

FN1. Claims 1 and 2 read as follows:

> 1. A method for preparing bacterial strains which produce aminoacids [sic] comprising combining a chromosome DNA fragment of a donor bacterium containing genes controlling the synthesis of a selected aminoacid and having a mutation which destroys the negative regulation of the synthesis of said aminoacid, with a plasmid DNA molecule capable of ensuring amplification, to form a hybrid DNA molecule; transforming with said hybrid DNA molecule, cells of a recipient bacterial strain having a mutation blocking the synthesis of the selected aminoacid in said strain and a mutation partly blocking the related step of metabolism of said aminoacid, to yield a bacterial strain possessing increased productivity of the selected aminoacid.
>
> 2. A method as claimed in claim 1,

wherein for the removal of ballast genetic material, the hybrid DNA molecule is treated, prior to transforming cells of the recipient strain, with specific endonucleases ensuring cleavage of the hybrid molecule of DNA in predetermined sites of the molecule, followed by recombination and joining of the required DNA fragments with polynucleotide ligase.

FN2. Claims 3 and 4 provide as follows:

3. A method as claimed in claim 1 for preparing a strain which produces L-threonine, wherein a fragment of the chromosome DNA of the donor strain *E. coli* VNIIGenetika MG442, produced by means of the endonuclease Hind III containing genes of threonine operon which as a result of mutation is insensitive to inhibition by threonine is combined with plasmid pBR322 to form a hybrid plasmid having a molecular weight of 11.4 Megadaltons, consisting of two copies of the plasmid pBR322 and said chromosome DNA fragment of the donor strain; said hybrid plasmid transforming cells of the recipient strain *E. coli* VL334 having mutations blocking the synthesis of L-threonine and L-isoleucine, the blocking with respect to isoleucine being partial; wherein the strain *E. coli* VNIIGenetika VL334(pYN6) which produces L-threonine is obtained and identified by registration number CMIM B-1649.

4. A method as claimed in any of claims 1 or 2 for preparing a strain which produces L-threonine, wherein a fragment of the chromosome DNA of the donor strain *E. coli* VNIIGenetika MG442, produced by means of the endonuclease Hind III containing genes of threonine operon which as a result of mutation is insensitive to inhibition by threonine is combined with plasmid pBR322 to form a hybrid plasmid with a molecular weight of 11.4 Megadaltons, consisting of two copies of the plasmid pBR322 and said fragment chromosome DNA of the donor strain; said hybrid plasmid being treated with endonucleases Hind III and Bam HI and the obtained fragments recombined and joined by treating same with polynucleotide ligase; said treated hybrid plasmid having a molecular weight of 5.8 Megadaltons, and consisting of one molecule of the plasmid pBR322 and said chromosome DNA fragments of the donor strain, ensuring resistance of the resulting cells against penicillin and may be contained in cells at the stage of logarithmic growth in an amount of about 20 copies; transforming with said treated hybrid plasmid, cells of the recipient strain *E. coli* VL334 having mutations blocking the synthesis of L-threonine and L-isoleucine, the blocking of isoleucine synthesis being partial; wherein the strain *E. coli* VNIIGenetika VL334(pYN7) which produces L-threonine is obtained and identified by the registration number CMIN B-1684.

Claim 1 of the '765 patent teaches a two-step process of combining and transforming. First, a chromosome FN3 DNA fragment of a donor bacterial strain is combined with a plasmid FN4 DNA molecule to form a hybrid DNA molecule. (D.I. 194, Ex. A, col. 12, lines 1-9) The chromosomal piece of DNA from the donor bacterial strain, which is part of the hybrid DNA molecule, has two characteristics: (1) it contains the instructions (or genes) for the production of the selected amino acid (i.e., the amino acid operon); and (2) its genetic structure has been changed (or mutated) to eliminate the negative regulation of the synthesis of the amino acid (i.e., the feedback resistant amino acid operon has been destroyed). (D.I. 194, Ex. A, col. 12, lines 4-7) This hybrid DNA molecule is then transformed (or inserted) into a recipient bacterial strain. The recipient

bacterial strain also has two characteristics: (1) its genetic structure has been changed (or mutated) so that it cannot produce the selected amino acid; and (2) its genetic structure has been changed (or mutated) so that it can only partially break down (or metabolize) the amino acid. (D.I. 194, Ex. A, col. 12, lines 11-14) The resulting combination of the hybrid DNA molecule and the recipient bacterial strain has increased production capability of the selected amino acid. (D.I. 194, Ex. A, col. 12, lines 14-15) The process taught in claim 1 utilizes three major components: (1) a chromosome DNA fragment from a donor bacterial strain; (2) a plasmid DNA molecule; and (3) host cells as the DNA recipient.

> FN3. A "chromosome" is a large molecule consisting of discrete segments of DNA called genes, which are arranged end-to-end like links of a chain and provide the genetic information necessary for cell life.
>
> FN4. A plasmid is usually a small circular DNA molecule which can act as a carrier of other DNA inside a cell. Plasmids exist independently of the chromosome DNA of the cell and may be present in many copies in a single bacterial cell. Under most circumstances, plasmids are not necessary for cell life.

Amino acids are the building blocks of proteins. Proteins are one of the basic groups of chemicals necessary for life because they are required for cell growth and reproduction. There are twenty amino acids: alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan, glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine, aspartic acid, glutamic acid, lysine, arginine, and histidine. *In re O'Farrell*, 853 F.2d 894, 896 n. 20 (Fed.Cir.1988). A bacterial strain is a type or variety of a particular species of bacteria. There are thousands of known species of bacteria, as well as many bacterial strains within each species. All bacteria naturally make amino acids.

***2** As recognized by the patent, "[a]minoacids [sic] produced by microorganisms find extensive use as feedstuff and food additives in the agriculture and food industry...." (D.I. 194, Ex. A, col. 1, lines 8-12) The '765 patent specifically discloses a method for making *Escherichia coli* ("*E. coli* ") bacteria capable of producing the amino acid threonine in increased quantities.[FN5] Threonine is an essential amino acid for many animals because it cannot be produced by the animal, but must be supplied through its diet. ADM's animal feed supplements supply various essential amino acids, including threonine.

> FN5. The patent specification first describes several experiments using *E. coli* in which the inventors used an unmutated donor chromosome DNA molecule in combination with a plasmid to form a hybrid DNA molecule. (D.I. 194, Ex. A, col. 6, lines 4-22) In these experiments, threonine production did not increase. The specification then sets forth Examples 1 and 2, describing the use of a mutated donor chromosome DNA molecule in combination with a plasmid to form a hybrid DNA molecule where threonine production increased. (D.I. 194, Ex. A, col. 8, line 45 through col. 10, line 53) In Example 3, the amount of threonine formed by the *E. coli* strains of Examples 1 and 2 is measured. (D.I. 194, Ex. A., col. 10, line 55 through col. 11, line 68)

The patent application which ultimately issued as the '765 patent on July 14, 1981 was filed in the United States Patent and Trademark Office ("PTO") by 14 Russian inventors on June 28, 1979. All of the inventors at the time of filing were employees of the All-Union Research Institute of Genetics and Selection of Industrial Microorganisms ("Genetika"). The inventors claimed a priority filing date based upon an application filed in the U.S.S.R. on June 30, 1978.

On January 21, 1980, during prosecution of the ap-

plication, the Patent Examiner rejected claims 1-4 as not enabled under 35 U.S.C. § 112 because, *inter alia*,"[a]pplicants fail[ed] to comply with requirements (1) and (3) of MPEP 608.01(p) Deposit of Microorganisms regarding the parent *E. coli* strains and the newly produced *E. coli* strains." (D.I. 64, Ex. B) At the time the application for the '765 patent was pending, § 608.01(p) of the Manual of Patent Examining Procedure ("MPEP") provided as follows:

Some inventions which are the subject of patent applications depend on the use of microorganisms which must be described in the specification in accordance with 35 U.S.C. 112. No problem exists when the microorganisms used are known and readily available to the public. When the invention depends on the use of a microorganism which is not so known and readily available, applicants must take additional steps to comply with the requirements of Section 112.

In the latter circumstances, the MPEP required applicants to make "a deposit of a culture of the microorganism in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted...." The section further provided that "all restrictions on the availability to the public of the culture so deposited will be irrevocably removed upon the granting of the patent." (D.I. 64, Ex. C) FN6

FN6. Since the '765 patent was prosecuted, the MPEP rule relating to the "[n]eed or opportunity to make a deposit" has been codified at 37 C.F.R. § 1.802.

In May 1980, in response to the Examiner's rejection, applicants agreed to "attempt to rectify depository deficiencies" by "furnishing a new declaration containing the required information." (D.I. 64, Exs. E, F at 16) On August 25, 1980, the applicants filed the declaration with the PTO, representing under penalty of perjury that,

no later than the effective U.S. filing date of the application, [they had] made a deposit of a culture of the microorganism in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted, under conditions which assure (a) that access to the culture will be available during pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122, and (b) that all restrictions on the availability to the public of the culture so deposited will be irrevocably removed upon the granting of the patent.

***3** This deposit is identified by: Deposit number CMIM B-1628, CMIM B-1641, CMIM B-1649, CMIM B-1684.

Name and address of the depository: Central Museum of Industrial Microorganisms of the All-Union Research Institute of Genetics and Selection of Industrial Microorganisms, USSR, Moscos 113545, Dorozhnaya S.

Taxonomic description (if available): Escherichia coli K-12.

(D.I. 64, Ex. G at 2) The donor strain (MG442) was registered as CMIM B-1628; the recipient strain (VL334) was registered as CMIM B-1641; the product of claim 3 (VL334(pYN6)) was registered as CMIM B-1649; and the product of claim 4 (VL334(pYN7)) was registered as CMIM B-1684. The examiner subsequently issued a Notice of Allowance and the '765 patent issued on July 14, 1981. In 1991, Ajinomoto was assigned all rights in the '765 patent.

B. Threonine Producing Bacterial Strains

As noted above, claims 3 and 4 of the '765 patent, although process claims, identify bacterial strains VL334(pYN6) and VL334(pYN7) respectively. (D.I. 261 at 1; D.I. 262 at 2) The bacterial strains that ADM uses to produce threonine are not these exact strains. Instead, ADM uses the strains identified as G472T23(pYN8), G472T23(pYNSTOP),

and G472T23(pYNTE2) to produce threonine. (D.I. 210 at 6) The relationship between the two original bacterial strains produced by Genetika and ADM's three strains is set forth below, to the best of the court's understanding.

After the filing of the application for the '765 patent, the inventors at Genetika continued to conduct research aimed at creating bacterial strains that are capable of overproducing threonine. By 1979, the Genetika inventors produced the bacterial strain M-1(pYN7) from the VL334(pYN7) bacterial strain. The inventors obtained U.S. Patent No. 4,321,325 ("the '325 patent") entitled "Process for Producing L-Threonine," for the method of producing threonine using the M-1(pYN7) strain. (D.I. 210, Ex. C, col. 8, lines 25-60; D.I. 262 at 3) The '325 patent explains that the M-1 bacterial strain was obtained by "inoculating to an agar-doped culture medium" the VL334(pYN7) strain. (D.I. 210, Ex. C, col. 8, lines 45-46) The M-1 strain is isolated from other individual colonies because it can produce L-threonine on "a minimal glucose-salt nutrient medium" and retains the plasmid PYN7 during the course of fermentation. (D.I. 210, Ex. C, col. 8, lines 46-51)

The inventors continued their research using the M-1(pYN7) strain. By 1992, the inventors obtained U.S. Patent No. 5,175,107 ("the '107 patent") entitled "Bacterial Strain of *Escherichia coli* BKIIM B-3996 as Producer of L-Threonine." (D.I.210, Ex. D) The '107 patent covers the bacterial strain *Escherichia coli* BKIIM B-3996 as the producer of L-threonine. The '107 patent includes a reference to an intermediate strain, G472T23(pYN7), derived from the M-1(pYN7) strain. (D.I. 210, Ex. D, col. 2, lines 25-33; D.I. 262 at 3) The G472T23(pYN7) bacterial strain is characterized in patent '107 as a mutant of the M-1(pYN7) strain that is capable of "utilizing saccharose and saccharose-bearing substrates, such as molasses, as a source of carbon." (D.I. 210, Ex. D, col. 2, lines 14-21) The G472T23(pYN7) is also different from the M-1(pYN7) strain in that it is resistant to both L-threonine and L-homoserine. (D.I. 210, Ex. D, col. 2, lines 29-31) The '107 patent sets forth two "stages" that produce the differences between the M-1(pYN7) strain and the G472T23(pYN7) strain. (D.I. 210, Ex. D, col. 2, lines 14-27) The first stage describes the process as follows: "[A] genetic determinant of saccharose assimilation is transferred to [the M-1(pYN7) strain] by virtue of transduction by bacteriophage P1 grown on a saccharose assimilating strain." (D.I. 210, Ex. D, col. 2, lines 14-17) The second stage describes the process as follows: "[S]pontaneously arisen mutants capable of growing on a minimal medium of M9, containing inhibitory concentrations of L-threonine (5 mg/L) are taken out of the saccharose-assimilating transformant." (D.I. 210, Ex. D, col. 2, lines 21-25) From this second "stage," the G472T23(pYN7) strain is isolated as one of the mutant strains.

***4** Through an agreement, the G472T23(pYN7) strain was transferred by Genetika to A.C. Biotechnics. (D.I. 210 at 6) The agreement also conferred to A.C. Biotechnics the right to practice the '765 patented process. (D.I. 210 at 6) ABP International AB ("ABP"),[FN7] a Swedish corporation, became the successor to A.C. Biotechnics. (D.I. 210 at 6) ABP conducted research to develop the bacterial strain G472T23(pYN8). The pYN8 plasmid in the ABP strain is different from the Genetika pYN7 plasmid because ABP restored the tetracycline resistant gene that was defective in the PYN7 plasmid. (D.I. 262 at 3) According to ADM, ABP's research resulted in the G472T23(pYN8) strain producing 80-90 g/L of threonine. (D.I. 210 at 6) ABP's research also produced two other strains, G472T23(pYNSTOP) and G472T23(pYNTE2). (D.I. 210 at 6) These two strains are different from Genetika's G472T23(pYN7) strain because ABP removed the "ampicillin resistance gene." (D.I. 262 at 3) According to ADM, the G472T23(pYNSTOP) and G472T23(pYNTE2) strains are capable of producing more threonine than the G472T23(pYN8) strain. (D.I. 210 at 6) ABP transferred the three strains it created from Genetika's G472T23(pYN7) strain to ADM. (D.I. 210 at 6) ADM uses these

three strains from ABP to produce threonine. (D.I. 210 at 6).

> FN7. ABP was originally joined as a defendant in this case. (D.I. 59) Ajinomoto filed a motion for default judgment when ABP did not respond to its complaint. (D.I. 148) The record indicates that ABP went into liquidation and ceased to exist as of April 29, 1996, and that service was not effected. (D.I. 180) Accordingly, on October 2, 1996, the court denied Ajinomoto's motion for default judgment.

III. CLAIM CONSTRUCTION

It is the court's "power and obligation to construe as a matter of law the meaning of language used in the patent claim." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed.Cir.1995), *aff'd*,116 S.Ct. 1384 (1996). This is so whether or not the parties formally dispute claim construction, because it is the court's duty to instruct the jury as to the law in connection with allegations of infringement. *Id.* at 981 (claim construction "ordinarily can be accomplished by the court in framing its charge to the jury, but may also be done in the context of dispositive motions such as those seeking judgment as a matter of law"). FN8

> FN8. For these reasons, Ajinomoto's motion for sanctions (D.I. 252) is denied. Although Ajinomoto chose to respond to ADM's claim construction motion by moving for sanctions rather than on the merits, the court will give Ajinomoto an opportunity to respond to the court's discussion prior to trial.

Courts are directed to consider three sources to ascertain the meaning of a claim: The literal language of the claim, the patent specification, and the prosecution history. When interpreting the words of the claim, the court should "ascribe [to the words] their ordinary meaning unless it appears the inventor used them otherwise." *Bell Communications Research Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 620 (Fed.Cir.1995). The words of the claim must be construed in the light of the specification, whose "description may act as a sort of dictionary, which explains the invention and may define terms used in the claims." *Markman*, 52 F.3d at 979. The court should also consider the patent's prosecution history, as it constitutes an "undisputed public ..." expression of what the patentee understood in terms of claim construction. *Id.* at 980. The court may, in its discretion, consider extrinsic evidence "to assist in its construction of the written document, a task it is required to perform." *Id.* at 981. "Extrinsic evidence consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Id.* at 980. Neither the patent's prosecution history nor any extrinsic evidence considered can "enlarge, diminish, or vary" the limitations in the claims. *Id.*

***5** In its motion for claim construction, ADM disputes the interpretations of various terms used in the '765 patent claims, as well as the interpretations of how one practices claims 3 and 4. The terms so disputed shall be addressed *seriatim.*

A. The Term "Chromosome DNA Fragment of A Donor Bacterium"

The claims of the '765 patent require that a "chromosome DNA fragment of a donor bacterium" or a "fragment of the chromosome DNA of a donor strain *E. coli* VNIIGenetika MG442" be used for combining with a plasmid DNA molecule to form a hybrid DNA molecule or hybrid plasmid. (D.I. 240, Ex. A, col 12, lines 1-48) According to ADM, "[b]acteria have two, or, at most, three types of DNA: chromosome DNA, plasmid DNA, and bacteriophage (or phage) DNA." (D.I. 240 at 7) ADM argues that chromosome DNA fragments cannot be equated with plasmid DNA fragments. (D.I. 240 at 7) ADM seeks this limitation in response to the following language from Ajinomoto's expert report:

I have also been asked to provide my opinion

whether a method of making a strain in which the threonine operon-containing insert is transferred into a Mu bacteriophage which would then incorporate itself into the *E. coli* chromosome. As a result, the hybrid bacteriophage would no longer be present in the end product strain but would function exactly as if the plasmid were present. In my opinion, these genetic manipulations and resulting strains directly infringe or are substantially the same as the claims of the '765 patent for the following reasons. First, the feedback resistant threonine genes originate in the bacterial chromosome. Second, those genes are combined with a genetic element that, like a plasmid, is capable of amplification and replication independent of the chromosome. Finally, the hybrid is introduced into a host strain that is auxotrophic for threonine and has a mutation partly blocking a related step of metabolism.

(D.I. 240, Ex. B at ¶ 51) ADM argues that Ajinomoto's expert equates a chromosome DNA fragment with a plasmid DNA fragment because he apparently believes that "once a chromosome fragment, always a chromosome fragement-even when the fragment has been part of a plasmid for ten years or more." [FN9] (D.I. 240 at 7)

> FN9. It is unclear to the court, based on the record, whether a fragment of chromosome DNA from a hybrid plasmid that was formed by combining a chromosome DNA fragment and a plasmid DNA fragment retains its identity as a chromosome DNA fragment or whether it assumes a new identity either as a hybrid plasmid DNA fragment or a plasmid DNA fragment. Furthermore, it is unclear whether the amount of time that a chromosome DNA fragment is part of a hybrid plasmid is relevant to the identification of DNA fragments from the hybrid plasmid.

ADM supports its position that the term "chromosome DNA fragment of a donor bacterium" should not be interpreted to include the term "plasmid DNA fragment" or "bacteriophage DNA fragment" by reference to the '765 specification and definitions in a treatise on biochemistry.[FN10] The term "chromosome" is not defined in the '765 specification. The treatise that ADM cites defines "chromsome" as "a single large DNA molecule containing many genes and functioning to store and transmit genetic information." (D.I. 240, Ex. C at 970) The treatise defines "plasmids" as "[a]n extrachromosomal, independently replicating small circular DNA molecule." (D.I. 240, Ex. C at 977) The '765 patent specification defines the term "plasmid" as "genetic elements reproducing in bacterial cells irrespective of chromosomes." (D.I. 240, Ex. A, col. 1, lines 16-17) The '765 patent also does not define the term "bacteriophage," but does make a reference to "plasmids" and "phages." The '765 patent specification states "[t]he term vector molecules denotes DNA molecules of plasmids and phages." (D.I. 240, Ex. A, col. 1, lines 23-24). The treatise defines bateriophage as "a virus capable of replicating in a bacterial cell." (D.I. 240, Ex. C at 970) The term "virus" is defined by the treatise as "a self-replicating, infectious, nucleic acid protein complex that requires an intact host cell for its replication and that contains a chromosome of either DNA or RNA." (D.I. 240, Ex. C at 980) ADM argues that, given the discussion of phage and plasmid in the '765 patent specification and the accepted terminology provided by the biochemistry treatise, the patent applicants could not have intended that the term "chromosome DNA fragment" includes DNA fragments from plasmids or phages. (D.I. 240 at 8) ADM asserts that nothing in the specification, prosecution history, or extrinsic evidence shows that the term "chromosome DNA fragment from a donor bacterium" includes DNA fragments from plasmids or phages. (D.I. 240 at 9)

> FN10. ADM cites to the following treatise: Albert L. Lehnigher, *Principles of Biochemistry* 969-980 (1982). (D.I. 240, Ex. C)

***6** Ajinomoto's expert Dr. Falkinham apparently

takes a different approach in defining the term "chromosome DNA fragment of a donor bacterium strain." Dr. Falkinham defines this term by first defining "donor bacterium" as "the bacterium with which a scientist begins the experiment; it contains the genes of interest." (D.I. 240, Ex. B at ¶ 30) He then defines "chromosome" as "the single DNA molecule carrying all the essential genes for the organism." (D.I. 240, Ex. B at ¶ 30) Finally, Dr. Falkinham defines "DNA fragment" as "a piece of DNA or genetic material that has been cut from another source using specific enzymes." (D.I. 240, Ex. B at ¶ 31)

Dr. Falkinham defines "plasmid" as "a host DNA molecule with the ability to replicate independently of the chromosome; it is typically circular." (D.I. 240, Ex. B at ¶ 36) The term "hybrid molecule" is defined as "the resulting DNA [which] is a combination of DNA from more than one different source." (D.I. 240, Ex. B at ¶ 37)

The court concludes that the term "chromosome DNA fragment" is limited to DNA from a chromosome, and does not include DNA fragments from either plasmids or bacteriophages, subject to the questions raised in footnote 9 *supra*.

B. The Terms "Plasmid" and "Phage"

ADM asserts that Ajinomoto's expert has interpreted the term "plasmid" as used in the '765 claims to cover the term "bacteriophage." (D.I. 240 at 9) ADM argues that there is no support in the '765 patent specification or prosecution history for this interpretation. The '765 patent specification defines the term "vector molecules" as "DNA molecules of plasmids and phages." (D.I. 240, Ex. A, col. 1, lines 23-24) ADM explains that a vector is a means of transporting certain biological material. (D.I. 240 at 9) ADM further explains that, in the molecular biology field, a vector DNA molecule is used to "carry" certain genes. (D.I. 240 at 10)

In supporting its position, ADM argues that the prosecution history specifically supports the interpretation that the term "bacteriophage" is not included in the definition of the term "plasmid." The '765 patent claims call for combining a chromosome DNA fragment with a plasmid DNA molecule to produce a hybrid DNA molecule or a hybrid plasmid. (D.I. 240, Ex. A, col. 12, lines 1-48) As originally submitted to the PTO, the term "vector" DNA molecule was used instead of the term "plasmid" DNA molecule as the element combined with the chromosome DNA fragment. (D.I. 240, Ex. D at 42) The patent examiner required the claims to be limited to plasmids, stating:

The disclosure is not enabling to support the breadth of the term "vector DNA molecule." Only plasmids appear to be suitable and operative as the vector.

(D.I. 240, Ex. D at 99) Accordingly, the patent applicants amended the claims of the '765 patent to delete the use of the term "vector" DNA molecule and replaced it with "plasmid" DNA molecule. (D.I. 240, Ex. D at 115)

***7** Based on this evidence and the '765 patent specification, the court concludes that the term "plasmid" cannot be interpreted to include the term "phage."

C. The Term "Amplification"

Claim 1 of the '765 patent calls for the plasmid DNA molecule to be "capable of ensuring amplification" of the genes controlling amino acid synthesis. (D.I. 240, Ex. A, col. 12, lines 8-9) ADM argues that the term "amplification" should be interpreted to mean any increase in the number of genes. (D.I. 240 at 10) To support this interpretation, ADM refers to the '765 patent specification that defines "amplification" to mean "increasing the number of genes in a cell." (D.I. 240, Ex. A, col. 1, lines 36-37) ADM seeks this interpretation because Ajinomoto's expert testified at deposition that the term "amplification" means increasing the number

of genes in the recipient cell by at least five. (D.I. 240, Ex. E at 225) Dr. Falkinham further testified that one skilled in the art would know this limitation because of published scientific literature. (D.I. 240, Ex. E at 226)

The court concludes that since the '765 patent specification clearly defines "amplification" to mean any increase in the number of genes, the term should not be interpreted to require a minimum increase, such as a five gene increase.

D. The Term "Hybrid DNA Molecule"

In the '765 patent claims, the term "hybrid DNA molecule" (sometimes referred to as a "hybrid plasmid" in the specification and in claims 3 and 4) is defined as being produced by combining a chromosome DNA fragment with a plasmid DNA molecule. ADM argues that the term "hybrid DNA molecule" should be interpreted to mean molecules that are made by both "in vivo" and "in vitro" methods.[FN11] (D.I. 240 at 11) Ajinomoto has argued that only hybrid DNA molecules made in vitro can be considered to fall within the scope of the claims of the '765 patent. (D.I. 191 at 15) ADM claims that the '765 patent specification makes references to both in vivo and in vitro preparation of hybrid molecules. (D.I. 240 at 12)

> FN11. "In vitro" refers to events that occur in a test tube, while "in vivo" refers to events that occur in a cell or organism. (D.I. 240, Ex. C at 974)

The court notes, however, that the reference to in vivo preparation of hybrid molecules in the '765 patent specification appears in a discussion of another patent:

> Certain practical aspects of applying of [sic] genetic engineering methods are revealed in the method for preparing the strains Pseudomonas involving degradation of complex organic compounds (petroleum hydrocarbons) (cf. U.S.Pat. No. 3,923,603) This patent teaches in vivo preparation of hybrid molecules by way of intracellular recombination.
>
> However, methods of preparing strains producing aminoacids [sic] with the use of genetic engineering techniques are hitherto unknown.

(D.I. 240, Ex. A, col. 2, lines 59-68) Given this limited reference to in vivo methods, the court concludes that the term "hybrid DNA molecule" refers only to molecules prepared in vitro.

E. The Term "Metabolism"

Claim 1 of the '765 patent calls for the recipient strain to be mutated so that "metabolism" of the selected amino acid is partly blocked. (D.I. 240, Ex. A, col. 12, lines 10-14) ADM argues that the term "metabolism" should be interpreted to mean the "breaking down and synthesis of molecules" and cites two scientific treatises for support.[FN12] (D.I. 240 at 13) Ajinomoto has argued that the term "metabolism" should be interpreted to mean only the breaking down of molecules and that the synthesis of complex molecules, such as proteins from amino acids, should not be included in the term "metabolism." (D.I. 221 at 180-182)

> FN12. ADM relies on: Albert L. Lehninger, *Principles of Biochemistry* 975 (1982) and William T. Keeton, *Biological Science*, A10 (3rd ed. 1980). (D.I. 240, Ex. C and F)

***8** The '765 patent specification does not define the term "metabolism.", The language of the '765 patent claims, however, makes a distinction between the term "synthesis" and the term "metabolism." For example, in claim 1 the recipient bacterial strains are described as having a "mutation blocking the synthesis of the selected" amino acid and a "mutation partly blocking the related step of metabolism of said" amino acid. (D.I. 240, Ex. A, col. 12, lines 10-14) (emphasis added). In claims 3 and 4, the recipient bacterial strain VL334 is described as having a mutation blocking the synthesis of L-

threonine and a mutation partly blocking the synthesis of L-isoleucine. (D.I. 240, Ex. A, col. 12, lines 35-37 and 62-65) The distinction between the term "synthesis" and the term "metabolism" is also supported by the patent specification. (D.I. 240, Ex. A, col. 5, lines 1-65) Since the patent applicants chose to make distinctions between the terms "synthesis" and "metabolism" in the patent claims and specification, it appears that they intended the term "metabolism" to mean only the breaking down of molecules. Consequently, although the treatises cited by ADM define "metabolism" to mean the breaking down and synthesis of molecules, the court construes the term "metabolism" in the '765 patent to mean only the breaking down of molecules.

F. The "Practice" of Claims 3 and 4

ADM seeks interpretations of how one practices claims 3 and 4. ADM argues that to practice claims 3 or 4 requires the use of the specific donor strain, the specific recipient strain, and the specific hybrid plasmids mentioned in each claim. ADM also argues that to practice claims 3 or 4 requires the resulting bacterial strain to be the same bacterial strain mentioned in the claims.

Claim 3 is dependent on claim 1. Claim 3 identifies the donor strain as VNIIGenetika MG442 and the recipient strain as VL334. The hybrid plasmid is identified as pYN6, "having a molecular weight of 11.4 Megadaltons, consisting of two copies of the plasmid pBR322." The specification describes the plasmid pBR322, used to create the plasmid pYN6 as having "genes of resistance to ampicillin/-penicillin (Ap') and tetracycline (Tc')." (D.I. 240, Ex. A, col. 8, lines 54-56) The specification also describes cells containing the pYN6 plasmid as being resistant against the tetracycline. (D.I. 240, Ex. A, col. 9, lines 44-47) The resulting bacterial strain is identified in claim 3 as VL334(pYN6). The specification describes the VL334(pYN7) strain as being resistant against penicillin and tetracycline, and capable of growing on a medium without amino acids. (D.I. 240, Ex. A, col. 10, lines 2-4)

Claim 4 is dependent on claims 2 and 3. Claim 4 identifies the donor strain as VNIIGenetika MG442 and the recipient strain as VL334. (D.I. 240, Ex. A, col. 12, lines 41-62) The hybrid plasmid is identified as pYN7, "with a molecular weight of 11.4 Megadaltons, consisting of two copies of the plasmid pBR322." (D.I. 240, Ex. A, col. 12, lines 48-50) Claim 4 also describes a "treated hybrid plasmid" pYN7 as having "a molecular weight of 5.8 Megadaltons ..., ensuring resistance of the resulting cells against penicillin and may be contained in cells at the stage of logarithmic growth in an amount of about 20 copies...." (D.I. 240, Ex. A, col. 12, lines 54-61) Claim 4 identifies the resulting strain as VL334(pYN7). The specification describes the VL334 (pYN7) strain as being "resistant against penicillin and capable of growing in a medium without amino acids." (D.I. 240, Ex. A, col. 10, lines 45-48)

***9** ADM argues that since the claims 3 and 4 mention specific donor and recipient strains, specific hybrid plasmids, and a specific resulting bacterial strain, the claims should be construed such that practicing the claims requires the use of these specific materials. Ajinomoto seems to have argued throughout its pretrial motions that ADM's strains should be held to infringe claims 1-4 of the '765 patent so long as they have not been "materially changed." (See, e.g., D.I. 240, Ex. B at ¶¶ 47, 50)

The court will defer its decision on claims 3 and 4 pending further submissions from the parties.

IV. STANDARD OF REVIEW

Summary judgment should be granted only if a court concludes that "there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed.R.Civ.P. 56(c). The moving party bears the burden of proving that no genuine issue of material fact is in dispute. *Matsushita Elec. Indus. Co., Ltd. v. Zenith*

Radio Corp., 475 U.S. 574, 586 n. 10 (1986). Once the movant has carried its initial burden, the non-moving party "must come forward with 'specific facts showing that there is a genuine issue for trial.' " *Id.* at 587. "Facts that could alter the outcome are 'material,' and disputes are 'genuine' if evidence exists from which a rational person could conclude that the position of the person with the burden of proof on the disputed issue is correct." *Horowitz v. Federal Kemper Life Assurance Co.*, 57 F.3d 300, 302 n. 1 (3d Cir.1995) (citations omitted). This court must "view the underlying facts and all reasonable inferences therefrom in the light most favorable to the party opposing the motion." *Pennsylvania Coal Ass'n v. Babbitt*, 63 F.3d 231, 236 (3d Cir.1995) (citation omitted).

V. ANALYSIS

Both parties have moved for summary judgment on the issues of infringement and willfulness. (D.I. 89, 185) Likewise, both parties have moved for summary judgment on the issues of invalidity. More specifically, plaintiff Ajinomoto has moved for summary judgment on ADM's affirmative defenses that the '765 patent is invalid and unenforceable, contending in this regard that the '765 patent is enabled under 35 U.S.C. § 112 and nonobvious under 35 U.S.C. § 103. (D.I. 188) Defendant ADM, in its motions for summary judgment (D.I. 63, 182, 191, 193), contends that the '765 patent is invalid pursuant to 35 U.S.C. §§ 103 and 112. These issues will be addressed *seriatim.*

A. Infringement

It is undisputed in this case that ADM does not practice in the United States the process taught in the '765 patent. Prior to 1988, a patentee holding a process patent had no cause of action against a person who, having used the patented process abroad to manufacture products, proceeded to import, use or sell the products in this country.

In 1988, Congress enacted the Process Patent Amendments Act to address this perceived loophole. As codified in 35 U.S.C. § 271(g), Congress made it an act of infringement "to import into the United States, or to sell or use within the United States 'a product which is made by a process patented in the United States ... if the importation, sale, or use of the product occurs during the term of such process patent.' " *Eli Lilly and Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1572 (Fed.Cir.1996) (quoting § 271(g)). In response to a concern about the reach of the legislation to "other than the direct and unaltered products of patented processes,"*id.*, Congress further provided that a product, even if "made by" a patented process within the meaning of the statute, would "not be considered to be so after (1) it is materially changed by subsequent processes; or (2) it becomes a trivial and nonessential component of another product." 35 U.S.C. § 271(g).FN13

> FN13. Section 271(g) specifically provides, in relevant part, that "[w]hoever without authority imports into the United States or offers to sell, sells or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer...." ADM argues that § 271(g) is inapplicable to the facts of this case because ABP was "authorized" to practice the patented process outside the United States. The court rejects this argument as contrary to the plain language and the underlying purpose of the statute. None of the cases which have addressed § 271(g) have focused on whether the foreign act of production (i.e., practice) was authorized-the proper focus of § 271(g) is on the domestic act of importation, sale, or use. ADM clearly has imported, sold and/or used the products at issue in the United States without authority.

***10** The "materially changed" clause of § 271(g), while not specifically defined in the statute, must

be construed in light of the underlying purpose of the legislation, "which is to protect the economic value of U.S. process patents to their owners." *Eli Lilly*, 82 F.3d at 1572. As characterized by the Federal Circuit in the above referenced case, "Congress was concerned with the problem of the overseas use of patented processes followed by the importation of the products of those processes, and a grudging construction of the statute could significantly limit the statute's effectiveness in addressing the problem Congress targeted." *Id.* In attempting to provide some useful guidance on the meaning of the "material change" clause, the Federal Circuit in *Eli Lilly* quoted from the report of the Senate Committee:

A product will be considered to have been made by a patented process if the additional processing steps which are not covered by the patent do not change the physical or chemical properties of the product in a manner which changes the basic utility of the product [produced] by the patented process. However, a change in the physical or chemical properties of a product, even though minor, may be "material" if the change relates to a physical or chemical property which is an important feature of the product produced by the patented process. Usually a change in the physical form of a product (e.g., the granules to powder, solid to liquid) or minor chemical conversion (e.g., conversion to a salt, base, acid, hydrate, ester, or addition or removal of a protection group) would not be a "material" change.

Id. at 1577 (quoting from S.Rep. No. 83, 100th Cong., 1st Sess. 49, 50 (1987)).

In the *Eli Lilly* case, plaintiff Lilly purchased U.S. Patent No. 4,160,085, claim 5 of which defined a method of producing enol cephem compounds, including what is called "compound 6," an enol cephem similar to the one Lilly used in its process for manufacturing cefaclor, a patented antibiotic. Defendant American Cyanamid imported cefaclor which was manufactured in Italy by another defendant, Biochimica Opos, S.p.A. The court found that to produce cefaclor from compound 6 required four discrete chemical steps. Lilly argued that because cefaclor was the only product of compound 6 that was sold in the United States market, the change in compound 6 resulting in cefaclor-"no matter how significant as a matter of chemical properties or molecular structure"-was not a "material change" for purposes of § 271(g). *Id.* at 1571. The court disagreed, concluding that "[t]he chemical properties of the two compounds are completely different, the 'basic utility' of the products is different, and the chemical structure of the two products is significantly different." *Id.* at 1577 (emphasis added).

The Federal Circuit in *Bio-Technology General Corp. v. Genentech Inc.*, 80 F.3d 1553 (Fed.Cir.), *cert. denied*,1996 WL 496320 (Oct. 7, 1996), having described the "material change" test as requiring, at a minimum, "that there be a real difference between the product imported, offered for sale, sold, or used in the United States and the products produced by the patented process,"*id.* at 1560 (emphasis added), made clear that the patentee must initially establish that the product at issue was in fact made by a process patented in the United States. As explained by the court, § 271(g)

***11** does not specify what products will be considered to have been "made by" the patented process, apparently because Congress wanted the courts to resolve this critical question of proximity to the product of the patented process on a case-by-case basis.

Id. at 1561. In this regard, the legislative history of § 271(g) provided:
In the biotechnology field it is well known that naturally occurring organisms contain within them particular genetic sequences composed of unique structural characteristics. The patented process may be for the process of preparing a DNA molecule comprising a specific genetic sequence. A foreign manufacturer uses the patented process to prepare the DNA molecule which is the product of the patented process. The foreign manufacturer inserts the

DNA molecule into a plasmid or other vector and the plasmid or other [vector] containing the DNA molecule is, in turn, inserted into a host organism; for example, a bacterium. The plasmid-containing host organism still containing the specific genetic sequence undergoes expression to produce the desired polypeptide. Even if a different organism was created by this biotech procedure, if it would not have been possible or commercially viable to make the different organism and product expressed therefrom but for the patented process, the [polypeptide] product will be considered to have been made by the patented process.

Id. (quoting from S.Rep. No. 83, 100th Cong., 1st Sess. 51 (1987).

In *Bio-Technology General Corp*, the patent claims were directed to a method of constructing a replicable cloning vehicle (e.g., a plasmid) capable, in a microbial organism, of expressing a particular polypeptide (e.g., human growth hormone or "hGH"). The alleged infringer manufactured hGH in Italy by recombinant DNA techniques and planned to import the product for sale in the United States. The question before the court was whether hGH was a product made by a process patented in the United States, even though the patented process was limited to producing a plasmid, not hGH. The court concluded that hGH was a product "made by" the patented process under § 271(g):

There is little doubt that the plasmid product of the claimed process and hGH are entirely different materials, one being more than materially changed in relation to the other. hGH is not a mere modification of the plasmid. However, ... [t]he legislative history precisely anticipated this fact situation and indicated Congress's intent that infringement of a process for making a plasmid is not to be avoided by using it to express its intended protein. Moreover, the '832 patent itself explicitly contemplates that the patented process will be used as part of an overall process for producing hGH; indeed, the patent discloses in detail how to make hGH by carrying out the claimed process and other necessary steps. Thus, it cannot be said as a matter of law that the production of hGH is too remote from the claimed process of making a replicable cloning vehicle.

***12** *Id.*

In the case at bar, it is Ajinomoto's burden to prove that ADM's product was "made by" the '765 patented process. ADM argues in its summary judgment motion of noninfringement that the record is devoid of such proof. While Ajinomoto claims that there is some relevant evidence on this issue,[FN14] it also asserts that it is entitled to rely on 35 U.S.C. § 295, which provides that the accused infringer's product is presumed to have been made by the patented process if the trial court finds that (1) a substantial likelihood exists that the product was made by the patented process, and (2) the patentee made a reasonable effort to determine the process actually used in the production of the product but was unable to so determine. "If the trial court makes these findings, the burden of establishing that the product was not made by the patented process is on the accused infringer." *Novo Nordisk v. Genentech*, 77 F.3d 1364, 1368 n. 6 (Fed.Cir.1996). If the initial hurdle is surmounted, it is ADM's burden to demonstrate that its products have been materially changed.

FN14. Ajinomoto provides three pieces of evidence to support this assertion. Ajinomoto points to deposition testimony by one of the inventors, Dr. Kozlov. Dr. Kozlov testified that "he feels" that all the threonine producing strains that he made at Genetika "fall within [the '765 patent]." (D.I. 262, Ex. A at 34) According to Ajinomoto, Dr. Kozlov's testimony establishes that the '765 patent was practiced in producing the VL334(pYN7), M-1(pYN7), and the G472T23(pYN7) strains.

Ajinomoto also points to documents by ADM and ABP which purportedly demonstrate that Genetika practiced the

> '765 patented process to produce the G472T23(pYN7) strain. (D.I. 262, Ex. B and C, an ABP L-Threonine Manual and an ADM document submitted to the Japanese Ministry of Fisheries, Forestry and Agriculture, respectively)
>
> Ajinomoto asserts that ABP also practiced the patented process in producing the G472T23(pYN8) strain. To support its position, Ajinomoto states that
>
> ABP practiced the "combining step" in forming pYN8 by taking the chromosomal fragment from pYN7 and combining it with another plasmid (lacking the ampicillin resistance gene). ABP practiced the "transforming step" by inserting pYN8 into G472-T23 to produce G472-T23 (pYN8).
>
> (D.I. 262 at 6)

The court cannot conclude from the record presented both that there is a substantial likelihood that ADM's strains-the "product"-were made by the patented process and that Ajinomoto made a reasonable effort to determine the process actually used by ABP, but was unable to do so. In reaching this conclusion, the court rejects as nonpersuasive the evidence presented by Ajinomoto regarding Genetika's practice-a single conclusory deposition question and answer of Dr. Kozlov and the recitations by ABP in its literature of Genetika's general representations. The court further finds the '325 and '107 patents relevant to the question and insufficiently addressed. The court holds that Ajinomoto is not entitled to the presumption afforded by § 295.

With respect to the question of "material changes," the court concludes that there are genuine issues of material fact as to whether the differences between the alleged product of the patented process and ADM's products are "real," "significant," and/or "complete."

B. Validity

"A patent is presumed valid, and the burden of proving invalidity, whether under § 112 or otherwise, rests with the challenger. Invalidity must be proven by facts supported by clear and convincing evidence." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed.Cir.1988), *cert. denied*,490 U.S. 1046 (1989). The issues of enablement and obviousness are questions of law; however, a determination of enablement or obviousness is based on factual inquiries. *See, e.g., In re Goodman,* 11 F.3d 1046, 1049-50 (Fed.Cir.1993); *B.F. Goodrich Co. v. Aircraft Braking Systems Corp.*, 72 F.3d 1577, 1582 (Fed.Cir.1996).

1. Enablement

a. By disclosure

ADM urges the court to find the '765 patent invalid as not enabled pursuant to 35 U.S.C. § 112 ¶ 1. That provision requires that a patent's specification

> contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same....

***13** Thus, "[t]o be enabling under § 112, a patent must contain a description that enables one skilled in the art to make and use the claimed invention." *Atlas Powder Co. v. E.I. duPont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed.Cir.1984). The fact that "some experimentation is necessary does not preclude enablement; the amount of experimentation, however, must not be unduly extensive." *Id.* The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art.... The test is not merely quantitative, since a

considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed....

Factors to be considered in determining whether a disclosure would require undue experimentation ... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed.Cir.1988). "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *Id.*

The most persuasive of the factual considerations tending to demonstrate nonenablement at bar is illustrated by juxtaposing the breadth of claim 1 (and the sheer number of possible combinations of strains and amino acids ostensibly covered by the claim) and the limited examples proffered by the inventors (covering a single bacterial strain and a single amino acid). Courts in similar circumstances have viewed such facts as instructive.

For instance, the claim at issue in *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.,* 927 F.2d 1200 (Fed.Cir.), *cert. denied,*502 U.S. 856 (1991), was a generic claim, "covering all possible DNA sequences that will encode any polypeptide having an amino acid sequence 'sufficiently duplicative' of EPO [FN15] to possess the property of increasing production of red blood cells." *Id.* at 1212. The district court found that over 3,600 different EPO analogs could be made by substituting at only a single amino acid position, and over a million different analogs could be made by substituting three amino acids. Significantly, the record included testimony by the head of plaintiff's EPO analog program that "he did not know whether the fifty to eighty EPO analogs Amgen had made 'had the biological propert[ies]" described in the invention. *Id.* at 1213.

> FN15. "EPO" or erythropoietin is a protein consisting of 165 amino acids which stimulates the production of red blood cells. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.,* 927 F.2d at 1203.

The Federal Circuit, having recognized that "it is not necessary that a patent applicant test all the embodiments of his invention" or include representative samples at all, nevertheless concluded that the claim was not enabled.

***14** Here, ... despite extensive statements in the specification concerning all the analogs of the EPO gene that can be made, there is little enabling disclosure of particular analogs and how to make them. Details for preparing only a few EPO analog genes are disclosed.... This "disclosure" might well justify a generic claim encompassing these and similar analogs, but it represents inadequate support for Amgen's desire to claim all EPO gene analogs. There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them....

Considering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with attendant uncertainty as to what utility will be possessed by these analogs, we consider that more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity. It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity. Under the circumstances, we find no error in the court's conclusion that the generic DNA sequences claims are invalid under Section 112.

Id. at 1213-14 (emphasis added).

The claimed invention in *In re Vaeck*, 947 F.2d 488 (Fed.Cir.1991), was directed to the use of genetic engineering techniques for production of proteins that are toxic to certain insects. The applicants described the claimed invention in generic terms and disclosed in their specification "two particular species of Bacillus ... as sources of insecticidal protein; and nine genera of cyanobacteria ... as useful hosts. The working examples relevant to the claims on appeal detail the transformation of a single strain of cyanobacteria.... *Id.* at 490. The PTO rejected the claims on enablement grounds, affirming the examiner's finding that

undue experimentation would be required of the art worker to practice the claimed invention, in view of the unpredictability in the art, the breadth of the claims, the limited number of working examples and the limited guidance provided in the specification. With respect to unpredictability, the examiner stated that "[t]he cyanobacteria comprise a large and diverse group of photosynthetic bacteria including large numbers of species in some 150 different genera.... The molecular biology of these organisms has only recently become the subject of intensive investigation and this work is limited to a few genera. Therefore the level of unpredictability regarding heterologous gene expression in this large, diverse and relatively poorly studied group of procaryotes is high...."

Id. at 492-93. The Federal Circuit likewise affirmed.

Taking into account the relatively incomplete understanding of the biology of cyanobacteria as of [applicants'] filing date, as well as the limited disclosure by [applicants] of particular cyanobacterial genera operative in the claimed invention, we are not persuaded that the PTO erred in rejecting claims 1-46 and 50-51 under § 112, first paragraph. There is no reasonable correlation between the narrow disclosure in [applicants'] specification and the broad scope of protection sought in the claims encompassing gene expression in any and all cyanobacteria.

***15** *Id.* at 495. *See also In re Goodman*, 11 F.3d at 1050 (the applicant's specification, which contained but a "single example of producing gamma-interferon in the dicotyledonus species, tobacco," did not contain sufficient information to enable the broad scope of the claims, which included monocotyledonous plants); *Morton Intern., Inc. v. Cardinal Chemical Co.*, 5 F.3d 1464, 1469-70 (Fed.Cir.1993) ("The fifty-odd examples in the patent obviously teach something, but the evidence shows that they did not teach what was allegedly defined in the claims."); *In re Wright*, 999 F.2d 1557, 1562-63 (Fed.Cir.1993) (finding that "the scope of the appealed claims [was] not enabled by the general description and the single working example in the specification," where the applicant attempted to claim "any and all live, non-pathogenic vaccines, which elicit immunoprotective activity in any animal toward any RNA virus") (emphasis in original).

In addition to the considerations discussed above, ADM proffers the expert testimony of Dr. Rudolph in support of its position. Dr. Rudolph averred in relevant part that

[a]s to each of the millions of bacterial strains, it would have required, and still does require, extensive independent research to identify and isolate the DNA molecule containing the mutated genes for the production of each and every selected amino acid as called for in claims 1 and 2, as well as to identify a suitable plasmid which is capable of introducing such genes into the selected bacterial species. This amount and type of experimentation would not have been routine as of 1979, when the application was filed in the United States, and is not routine now.

The research and development necessary to identify and isolate mutants in one donor bacterial strain for increasing the production of even one amino acid other than threonine or tryptophan, whether in E. coli or another bacterium, would be very significant

and would not have been routine in 1979 or even now.

(D.I. 194, Ex. O, ¶¶ 7, 8)

ADM also directs the court's attention to several publications which indicate that research efforts were ongoing regarding transformation techniques and the development of appropriate vectors or plasmids for bacterial strains other than *E. coli* and for amino acids other than threonine. (D.I. 194, Exs. C, D, E, N) Finally, ADM relies on evidence that Ajinomoto in the past argued before the PTO that the '765 patent does not enable the use of any microorganism other than *E. coli* or the production of amino acids other than threonine. (D.I. 194, Exs. F, G, H, I, J, K, L)

To counter the record compiled by ADM, Ajinomoto offers the expert testimony of Dr. Falkinham, who describes how, in 1978-79, a person skilled in the art would follow the teachings of the '765 patent. (D.I. 203, Ex. K) Ajinomoto concludes that the '765 patent, as a pioneering patent consistently found to be enabled by the PTO, should not be invalidated for lack of an enabling disclosure under § 112 on the summary judgment record presented at bar.

***16** The court agrees. ADM has not carried its burden to demonstrate by clear and convincing evidence that the '765 patent is not enabled by its disclosure. The Federal Circuit, in its enablement decisions, has emphasized that a patent's claims need not specifically exclude possible inoperative substances in order to be enabled, unless "the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention...." *Atlas Powder Co. v. E.I. duPont De Nemours,* 750 F.2d at 1576. Similarly, "[i]t is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art." *In re Vaeck,* 947 F.2d at 496; *Application of Angstadt,* 537 F.2d 498, 503 (C.C.P.A.1976).

The publications cited by ADM do indicate that research continued in practicing the method taught in claim 1 on bacterial strains other than *E. coli* and amino acids other than threonine. Given the thousands of combinations of strains and amino acids ostensibly covered by claim 1 and the relatively few examples cited by either party, the publications constitute insufficient evidence upon which to base any enablement conclusions. Nor does the enablement testimony of ADM's expert, Dr. Rudolph, particularly illuminate the issue, as it is general and conclusory. *See In re Wright,* 999 F.2d at 1563 ("[E]ach of these affidavits fails in its purpose because each merely contains unsupported conclusory statements as to the ultimate legal question"). Moreover, when Dr. Rudolph's enablement testimony is compared to his testimony on the issue of obviousness (D.I. 192, Ex. J; D.I. 203, Ex. C), the court is not convinced that either proposition is clear. While the court recognizes that a party may assume contrary legal positions, the contrary factual assertions supporting each such position must be considered as a whole and not categorized. Finally, given the PTO's relentless rejection of Ajinomoto's previous position on enablement, Ajinomoto's advocacy hardly constitutes clear and convincing evidence of nonenablement.

2. By deposit

As noted above, the placement of microorganism samples in a public depository "has been considered adequate to satisfy the enablement requirement of 35 U.S.C. § 112, when a written description alone would not place the invention in the hands of the public and physical possession of a unique biological material is required." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.,* 927 F.2d at 1210.

A deposit has been held necessary for enablement where the starting materials (i.e., the living cells used to practice the invention, or cells from which the required cells can be produced) are not readily available to the public. Even when starting materi-

als are available, a deposit has been necessary where it would require undue experimentation to make the cells of the invention from the starting materials.

***17** *In re Wands*, 858 F.2d at 735. For instance,

[w]hen a biological sample required for the practice of an invention is obtained from nature, the invention may be incapable of being practiced without access to that organism. Hence the deposit is required in that case. On the other hand, when ... the organism is created by insertion of genetic material into a cell obtained from generally available sources, then all that is required is a description of the best mode and an adequate description of the means of carrying out the invention, not deposit of the cells. If the cells can be prepared without undue experimentation from known materials, based on the description in the patent specification, a deposit is not required.

Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d at 1211.

Despite the fact that claim 1 of the '765 patent is a generic claim, the PTO apparently required deposits of the microorganisms identified in claims 3 and 4 and found enablement of all claims 1-4 based on the deposits. In subsequent years, in response to Ajinomoto's recurring argument that the '765 patent was not enabled because the deposits were not publicly available, the PTO consistently found that "the teaching [of the '765 patent] is considered sufficient to enable the ordinary skilled artisan to practice the [patented] technique even where the specific mentioned starting microorganisms and host microorganisms are not available. Access to analogous microorganisms are well known and access thereto is readily available." (D.I. 203, Ex. B; see also Exs. E, I, J)

For purposes of its outstanding motions, ADM asserts that the '765 patent is not enabled unless the deposits required by the original examiner have been maintained and are readily accessible to the public. ADM contends in this regard that the deposits are not readily accessible to the public, based on the failed attempt to obtain samples by Dr. Andrei Sibirny, Head of the Department of Biochemical Genetics of the Lviv Branch of the Institute of Biochemistry in Ukraine. (D.I. 64, Ex. H)

To require deposits of specific bacterial strains to enable a generic claim covering, in ADM's own words, thousands of bacterial strains, does not make sense to the court in the first instance. Given the conclusion by at least one examiner after the '765 patent issued that a deposit of biological material was not necessary for enablement, there remains a question as to whether a biological sample is required for the practice of this invention.[FN16]

FN16. The court specifically rejects ADM's estoppel argument in this regard. As explained in the very authorities cited by ADM, "[t]he doctrine of file wrapper estoppel precludes a patent owner in an infringement suit from obtaining a construction of a claim that would in effect resurrect subject matter surrendered during the course of proceedings in the Patent and Trademark Office. The estoppel applies most frequently where an applicant amends or cancels claims rejected by the Office as unpatentable in light of the prior art." 4 Chisum, *Patents* § 18.05 at 18-153 (1996) (emphasis added). *Accord Haynes Intern., Inc. v. Jessop Steel Co.*, 8 F.3d 1573, 1577-78 (Fed.Cir.1993) ("The essence of prosecution history estoppel is that a patentee should not be able to obtain, through litigation, coverage of subject matter relinquished during prosecution.") (emphasis added). Unless ADM is arguing that, by depositing the specific strains identified in claims 3 and 4, generic claims 1 and 2 were abandoned, ADM's estoppel argument is supported neither by the facts nor the law. The court routinely reviews examiners' conclusions as to patentability and does not believe that conclusions as to en-

> ablement fall outside the scope of this jurisdiction. *Cf.*37 C.F.R. § 1.802(c) ("The reference to a biological material in a specification disclosure or the actual deposit of such material by an applicant or patent owner does not create any presumption that such material is necessary to satisfy 35 U.S.C. 112 or that deposit in accordance with these regulations is or was required").

Neither does the present record demonstrate by clear and convincing evidence that the deposits initially made are not readily accessible to the public. There are genuine issues of material fact as to whether Dr. Sibirny's request of record was appropriately made and, if so, whether the failure to affirmatively respond was a matter of miscommunication, an attempt to circumvent the patent requirements, or a matter of the deposits' nonviability.

B. Best Mode

***18** Ajinomoto asserts in its motion for summary judgment that the inventors disclosed the best mode of practicing the '765 claimed invention. Section 112 provides in relevant part that "[t]he specification ... shall set forth the best mode contemplated by the inventor of carrying out his invention." The Federal Circuit has described the best mode requirement as having two components:

The first is a subjective one, asking whether, at the time the inventor filed his patent application, he contemplated a best mode of practicing his invention. If he did, the second inquiry is whether his disclosure is adequate to enable one skilled in the art to practice the best mode or, in other words, whether the best mode has been concealed from the public.... Our case law has interpreted the best mode requirement to mean that there must be no concealment of a mode known by the inventor to be better than that which is disclosed.

Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d at 1209-10.

It would appear from Ajinomoto's argument that the best mode of practicing the '765 invention requires that the bacterial host be characterized by the presence of a relA+ gene. (D.I. 189 at 10-11) The question remains whether one skilled in the art would recognize the importance of the relA+ gene from the specification, which admittedly did not explicitly disclose such. The court declines to enter summary judgment on this issue based on the record presented.

C. Obviousness

ADM moves for summary judgment on the grounds that claims 1 and 2 are obvious under 35 U.S.C. § 103 and that certain publications are prior art to the patent-in-suit. Ajinomoto moves for summary judgment asserting the contrary positions.

As noted above, obviousness under § 103 is a legal conclusion based on several factual inquiries: "(1) the scope and content of the prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the pertinent art; [FN17] and (4) secondary considerations, if any, of nonobviousness." *Uniroyal, Inc. v. Rudkin-Wiley Corp.,* 837 F.2d 1044, 1050 (Fed.Cir.), *cert. denied,*488 U.S. 825 (1988). Secondary considerations include "evidence of factors tending to show nonobviousness, such as commercial success of the invention, satisfying a long-felt need, failure of others to find a solution to the problem at hand, and copying of the invention by others." *B.F. Goodrich Co. v. Aircraft Braking Systems,* 72 F.3d at 1582. When obviousness is based on prior art references, "there must be a showing of a suggestion or motivation to modify the teachings" of those references. *Id.* "With respect to the prior art printed publications, these references must be enabling, thus placing the allegedly disclosed matter in the possession of the public." *In re Epstein,* 32 F.3d 1559, 1568 (Fed.Cir.1994). "[T]he burden of showing, by clear and convincing evidence, the invalidity of [patent claims] is especially difficult when the prior art was before the PTO examiner during the prosecution of

the application." *Hewlett-Packard Co. v. Bausch & Lomb Inc.*, 909 F.2d 1464, 1467 (Fed.Cir.1990). Although the burden of proving invalidity never shifts from the party challenging the patent, the inventors' failure to provide prior art to the PTO should be considered in deciding whether the challenging party has met its burden.

> FN17. For purposes of these proceedings, the person of ordinary skill in the art as of June 30, 1978 would have had a Ph.D. in microbial genetics, with at least three years or more of post-doctoral experience. This person would have had experience in biochemistry and molecular genetics, and would have been aware of microbial recombinant DNA technology in vivo and in vitro.

***19** The publications characterized by ADM as prior art include: (1) a doctoral thesis authored by David Tribe in December 1976 and entitled *Tryptophan Production by Escherichia coli: A Feasibility Study*, (the "Tribe thesis") (D.I. 192, Ex. B); (2) an article entitled *Construction and Molecular Cloning of Hybrid Plasmids Containing Definite Fragments of Escherichia coli DNA*, authored by Kozlov et al. (including the named co-inventors Kozlov, Rebentish and Debabov) and published in volume 12, no. 1 of the journal Molekulyarnaya Biologiya (January-February 1978) (the "Kozlov article") (D.I. 192, Ex. F); (3) two articles [FN18] authored by several of the named co-inventors of the '765 patent (Livshits, Shakulov, Gusyatiner and Zhdanova) appearing in the publication Genetica 14(6) (June 1978) (the "Genetica articles") (D.I. 192, Exs. G and H); (4) several abstracts published in a compilation of abstracts of contributed papers presented at the Third International Symposium on the Genetics of Industrial Microorganisms in Madison Wisconsin in June 1978, including: (a) an abstract of Dr. Tribe's thesis (No. 12); (b) an abstract submitted by several of the co-inventors of the '765 patent (No. 59) entitled *Effect of relA Mutation on the Level of Threonine Overproduction in a Regulatory Mutant of E. coli K-12;* (c) an abstract submitted by Debabov and other co-inventors of the '765 patent (No. 67) entitled *Studies on Hybrid Plasmids Containing Genes of E. coli Threonine Operon* (collectively the "3d GIM Abstracts") (D.I. 192, Ex. D); (5) an article by E. Johnson et al. entitled *Threonyl-Transfer Ribonucleic Acid Synthetase and the Regulation of the Threonine Operon in Escherichia coli*, which appeared in J. Bacteriology 129 in 1977 (the "Johnson article") (D.I. 192, Ex. K); and (6) an article authored by Clarke and Carbon entitled *Biochemical construction and selection of hybrid plasmids containing specific segments of the Escherichia coli genome*, which was published in Proc. Nat'l Acad. Sci. USA, Vol. 72, No. 11 in November 1975 (the "Clarke/Carbon article") (D.I. 192, Ex. L).

> FN18. The articles are entitled, respectively, *Investigation of the Allelic State of the relA Gene on the Phenotypic Expression of Mutations of Threonine and Isoleucine Auxotrophy: Communication I. Influence of the allelic state of the relA gene on Pheotypic expression of mutations of threonine and isoleucine auxotrophy in Escherichia coli K-12* and *Investigation of the function of the relA gene in the expression of amino acid operons: Communication II. Influence of the allelic state of the relA gene on oversynthesis of threonine by a mutant of Escherichia coli K-12 resistant to beta-hydroxynorvaline.*

The first issue which must be addressed is whether any or all of these publications should be characterized as "prior art." All of the references identified by ADM are within the field of microbial genetics, "the field of the inventor[s'] endeavor." *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 449 (Fed.Cir.1986), *cert. denied*,484 U.S. 823 (1987). The court finds that ADM has presented sufficient indicia of the availability of the Genetica articles. (D.I. 201, Ex. T at B-452) The court finds that the abstracts are not enabling and do not

constitute prior art. The court further finds genuine issues of material fact as to whether the Tribe thesis was publicly available (D.I. 192, Exs. B, D) FN19 and whether the Kozlov reference and the Genetica articles FN20 were properly disclosed to the PTO during prosecution of the '765 patent. (D.I. 201, Ex. T at B-452)

FN19. The court rejects the testimony of any witnesses not identified as such during the course of discovery.

FN20. Dr. Rudolph, in his expert report, treated the two Genetika articles as equivalent and thus cumulative of each other. (D.I. 201, Ex. Q at ¶ 15) Therefore, the citation to one or the other is sufficient. *Halliburton Co. v. Schlumberger Technology Corp.*, 925 F.2d 1435, 1440 (Fed.Cir.1991).

***20** The parties characterize the teachings of the various prior art publications differently, through argument and expert testimony. It is undisputed that none of the prior art publications, standing alone, renders the teachings of the '765 patent obvious. (D.I. 192 at 17-19) ADM nevertheless argues that when viewed together, all of the elements of claims 1 and 2 are found. From the record presented, the court cannot confirm this proposition and, therefore, cannot conclude that obviousness has been demonstrated by clear and convincing evidence.FN21

FN21. Moreover, there is evidence of factors tending to show nonobviousness, especially that of ADM's quest to purchase the '765 technology in light of the failure of alternative threonine-producing technologies. (D.I. 200, Exs. A-K)

D. Unenforceability

Ajinomoto in its motion for summary judgment argues that the '765 patent was not obtained by means of inequitable conduct. Inequitable conduct consists of an " 'affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive.' " *B.F. Goodrich Co. v. Aircraft Braking Systems*, 72 F.3d at 1584. "One alleging inequitable conduct must prove the threshold elements of materiality and intent by clear and convincing evidence." *Id.*

In the case at bar, ADM in its responses to discovery requests asserted that the Tribe thesis and the Kozlov and Genetica articles constitute prior art which was not properly disclosed to the PTO. Ajinomoto disputes the characterization of the Tribe thesis as prior art and further argues that the latter publications were disclosed to the PTO.

The court has found that there are genuine issues of material fact as to whether the Tribe thesis was publicly available and whether the Kozlov reference and the Genetica articles were properly disclosed to the PTO. The court further concludes that there are genuine issues of material fact as to the issue of intent to deceive.

V. CONCLUSION

The parties, in connection with the pending matters addressed herein, have presented hundreds of pages of documents on complex factual questions to a court just introduced to the underlying science. The sheer number of documents deemed necessary by the parties to demonstrate their respective positions is a prime indicator that the search for "clear and convincing" evidence is a formidable task and, indeed, the "clear and convincing" evidence has eluded the court on this record.

For the reasons stated, the court finds there are genuine issues of material fact in connection with each of the issues addressed by the parties in their respective summary judgment motions. Therefore, all such motions shall be denied.

D.Del.,1996.
Ajinomoto Co. Inc. v. Archer-Daniels-Midland Co.

Not Reported in F.Supp., 1996 WL 621837 (D.Del.)
(Cite as: Not Reported in F.Supp., 1996 WL 621837 (D.Del.))

Not Reported in F.Supp., 1996 WL 621837 (D.Del.)

END OF DOCUMENT